Ointments, Creams & Gels

Chapter 10

Ointments, Creams, Gels

- Semi-solid dosage forms intended for topical application
- Skin, eye, nasally, vaginally, rectally
- Majority for the effect of the therapeutic agent they contain
- Non-medicated—Physical Effects

  --protectant, emollient

  --lubricant

Topical Preparations

- Primarily Localized—Site of Application
  --rash, dry skin, etc.
- Underlying layers of skin—local drug penetration
- Usually sub-therapeutic quantities absorbed—However—Pregnancy, nursing can cause problems
- Some Topical Applications—Systemic
  --i.e. Transdermals

Topical vs. Transdermal

- **Topical dermatological product is designed to deliver drug into the skin in treating dermal disorders—Target site:**

  --Skin

- **Transdermal Drug Delivery System is designed to deliver drugs through the skin (percutaneous absorption) to the general circulation for systemic effects—Target site:**

  --Site other than the Skin

  --Must penetrate stratum corneum (10-15 microns thick) to deliver drug to capillary beds between epidermis (50-150 microns) and dermis

Topical Dosage Forms

- Ointments
- Creams
- Gels and Jellies
- Pastes
- Others described in text book

Ointments

Ointments

- **Ointments: "Unguents"**
- **<u>Definition:</u> Dosage form consisting of medicaments dissolved or dispersed in a suitable base of mineral, vegetable, or synthetic origin**

Ointment Uses

- **As an Emollient**

  --preparation that softens the skin without being absorbed
- **Protective Agent**

  --i.e. ZnO—protect the skin against environment (sun, wind) or other agents (bacterial, fungal, etc.)
- **Vehicles to deliver drugs locally to the skin, scalp, rectum, etc.**

Classification of Ointment Bases

- **I. Hydrocarbon (Oleaginous) Bases:**
  - **A. Anhydrous**
  - **B. Do not absorb water readily (Hydrophobic)**
  - **C. Insoluble in water**
  - **D. Not washable**
  - **E. Examples—White Petrolatum, Plastibase, White Ointment, Yellow Ointment (Bees Wax)**
- **II Absorption Bases:**
  - **A. Anhydrous**
  - **B. Will absorb water (Hydrophilic)**
  - **C. Insoluble in water**
  - **D. Most are not washable**
  - **E. Examples—Anhydrous Lanolin, Hydrophilic Petrolatum, Aquaphor**

Classification of Ointment Bases

- **III. Emulsion Bases:**
  - **A. Emulsion Ointment Base (W/O):**
    1. **Hydrous**
    2. **Will absorb water**
    3. **Insoluble in water**
    4. **Not washable**
    5. **Water-Oil-Emulsion**
    6. **Examples—Lanolin, Rose water Ointment, Cold Cream**
  - **B. Emulsion Ointment Base (O/W):**
    1. **Hydrous**
    2. **Will absorb water**
    3. **Insoluble in water**
    4. **Washable**
    5. **Oil-in-Water Emulsion**
    6. **Hydrophilic Ointment, Velvachol, Unibase**

Classification of Ointment Bases

- **IV. Water-Soluble Bases:**
  - **A. Anhydrous**
  - **B. Will absorb water**
  - **C. Soluble in water**
  - **D. Washable**
  - **E. Greaseless**
  - **F. Examples—Polyethylene Glycol Ointment**

Hydrocarbon (Oleaginous) Bases

- **Description & Characteristics: See previous slides**
- **<u>Examples</u>:**

--Petrolatum, USP (Yellow Petrolatum, Petroleum Jelly)

-Commercial Product—Vaseline® (Chesebrough-Ponds)

(Mixture of Hydrocarbons)

--White Petrolatum, USP (White Petrolatum Jelly)

-Commercial Product—White Vaseline

--Yellow Ointment, USP (Simple Ointment)

-Yellow Wax (BeesWax)	**5%**
-Petrolatum	**95%**

Hydrocarbon (Oleaginous) Bases

- **Examples, cont.**

--White Ointment, USP

-White Wax (Purified Bees Wax) 5%

-White Petrolatum 95%

--Paraffin

-Purified mixture of solid hydrocarbons from petrolatum—Not a Base—

-Used to Stiffen Bases

--Mineral Oil (Liquid Petrolatum)

-Mixture of liquid hydrocarbons from petrolatum—Not a Base—

-Used to "Levigate" substances

--Plastibase (Used to be a Squibb product—now "licensed" by CLA)

--Low Mol. Wt. Polyethylene 5%

-Mineral Oil 95%

Absorption Bases

- **Description & Characteristics: See previous slides**
- **Examples:**

--Hydrophilic Petrolatum, USP

-Composed of Cholesterol, Stearyl Alcohol, White Wax and White Petrolatum

--Anhydrous Lanolin, USP (Refined Wool Fat)

-Contains <0.25% Water

-Insoluble in water

--Aquaphor

-Not an emulsion—Added to preparation to help form an emulsion; cholesterol, lanolin and white petrolatum

-Capacity to absorb up to 3 times its weight in water

Emulsion Bases

- **W/O Emulsion Ointment Base**
- **Examples:**

  --Cold Cream, USP

  --Rose Water Ointment (Old Cold Cream Formula

  --Lanolin, USP—May incorporate additional water into by mixing

Emulsion Bases

- **O/W Emulsion Ointment Base**
  - "Water-Removable Base"
- **Examples:**

--Hydrophilic Ointment, USP

-PG, Stearyl alcohol, White Pet, MP, PP, SLS, Purified Water

--Velvachol

--Unibase

Water Soluble Bases

- **Description & Characteristics: Previous Slides**
- **Examples:**

--Polyethylene Glycol Ointment, USP

-PEG 3350 400g

-PEG 400 600g

--Water soluble drugs can be absorbed into this base

--If 6 to 25% of an aqueous solution is to be incorporated, the USP allows substitution of 50 g of the PEG 3350 with an equal amount of stearyl alcohol in order to render the final product firmer, more viscous

Methods of Incorporation of Drugs into Ointment Bases

- **Insoluble Medicaments:**
- **A. Small amount of drug (<1%):**

Rx: Hydrocortisone 1% (0.5g)
White Petrolatum qs 50 g

--Drug is finely subdivided

--Use levigation– (form paste of drug + small amount of liquid; powder is insoluble; triturate until smooth)

--Dilute using geometric dilution with White Pet. (0.5g Drug + 1 g M.O. + 48.5 g White Pet)

Methods of Incorporation of Drugs into Ointment Bases

- **B. Large Amount of Drug (>15%):**

Rx: Zinc Oxide		**7 g**
Calamine		**8 g**
White Petrolatum	**qs**	**100 g**

--Problem—Cannot use Mineral Oil as levigating agent due to high powder content

--Therefore: Melt 30 g White Pet. (Use as lev. agent)

--Add remaining White Pet. By Geometric Dilution

Methods of Incorporation of Drugs into Ointment Bases

- **C. Liquids:**

Rx: Burrows Solution 2%
White Petrolatum qs 100%

--Incorporate liquid into <u>Absorption Base</u>
(Which one for W/O?)
--Add 2 ml Burrow's Soln to 3-4 g Abs Base
(Do not forget to account for Abs Base used)
--Add remaining White Pet. By Geometric Dilution

Methods of Incorporation of Drugs into Ointment Bases

- **Incorporation of Water-Soluble Drugs:**

Rx: Sodium Chloride 1%
White Petrolatum qs 100 g
--Dissolve drug in water (1g/5ml)
--Incorporate into Absorption Base (5 ml + 15 g Absorption Base)
--Qs with White Pet. by geometric dilution

Rx: Iodine 1%
White Petrolatum qs 100 g
--For Iodine, add Two Times amount of Potassium Iodide and dissolve in water (I_2 + KI --> KI_3)
--Incorporate into Absorption Base
--Qs with White Pet. by geometric dilution

Methods of Incorporation of Drugs into Ointment Bases

- **Granular or "Lumpy" Materials:**

Rx:	**Sulfur**		**2%**
	Salicylic Acid		**3%**
	White Petrolatum	**qs**	**50 g**

--Triturate Sulfur and Salicylic Acid in Mortar

--Melt 10 g White Pet.—Use as Levigating agent

--Qs with White Pet. by geometric dilution

Preparation of Ointments

- **Use Levigating Agents:**

  --MO, Water, PG, PEG, Glycerin—Several drops, not more than 2 ml

  --Eliminates clumping of powders

  --Improves homogeneity of powder dispersed in ointment base

  --Example of water soluble drug: Dissolve in portion of water—Mix Drug Solution into Absorbable Base—Continue by Geo. Dilution

  --Note: If you use Water, add excess. Water evaporates & Drug may crystallize out

- **General Guidelines:**

  --Never use Volatile Solvents as levigating agents, i.e.. Ether—If mix Salicylic Acid with volatile solvent and incorporate in Pet., will crystallize out

  --Combine powders and liquids and the ointment base by Geometric Dilution

  --Use a steel spatula with a wide blade, the size of which is proportional to the quantity of ointment being prepared

Preparation of Ointments by Pharmacists

- **Note: Choice of methods depends on the type of ingredients used (i.e. Heat labile drugs)**
- **Incorporation Method—Mechanical**

  --Most frequently used

  --Remember—Final Product must be uniform, homogenous, smooth, non-granular
- **Small Scale**

  --Spatula, Ointment slab (Pill Tile), or Nonabsorbent Parchment paper for smaller amounts of powders/liquids
- **Larger Scale**

  --Mortar & Pestle?

Preparation of Ointments

- General Guidelines, cont.:
- Use Plastic Spatula for Products with:
  --Tannic Acid
  --Mercury Salts
  --Iodine
  (these are corrosive to metal)
- Large Scale—Industry, etc.
  --Use Mechanical Ointment Roller Mills
  --Produces smooth, uniform ointments

Manufacturing Equipment

Ointment Mill

Electric Mortar and Pestle

Preparation of Ointments

- **Fusion Method:**

--Ingredients are combined by melting together and cooled by constant stirring until congealed (Ex: High m.p. Waxes such as Stearyl Alcohol, White Wax, Cetyl Alcohol, Yellow Wax, PEG 3350 to 20K)

--Useful Method if Drug is:

-Heat Stable

-Soluble in Melted Ointment Base

--Do not use if:

-Drug is Heat Labile (Thermal degradation)

-Contains Volatile Components (i.e. Menthol, Camphor, Thymol)

--Combine ingredients first, then heat—The solvent action lowers temp. necessary to melt them – OR melt highest MP wax first, then cool and add lower MP waxes

--ALWAYS use minimum amount of heat – Also can melt highest MP wax first, then cool and add lower MP waxes

Geometric dilution of drug with base

Levigate with small amount of base

Mix in well

Add second part

Mix in well and continue geometric dilution

Mix well until homogeneous

Other Problems with Compounding Ointments

- **Antibiotics:**

  --Most are unstable in the presence of moisture

  --Use Anhydrous Ointment Base

  (i.e. Petrolatum rather than Emulsion Type)

  --Specific Examples:

  -Penicillin—Do not put in ointment

  -Bacitracin—Inactivated by PEG Base

  -Polymixin—Stable in PEG esters

Other Problems with Compounding Ointments

- **Alkaloids: (atropine, atropine sulfate, scopolamine)**

  --Can be incorporated as salt or free alkaloid

  --If Salt, dissolve in small amount of water—Take up into Absorption Base (Aquaphor or Refined Wool Fat)

  --There is usually a Heat Stability Problem

- **Alcoholic Liquids (i.e. Tinctures):**

  --If volume is large, partially evaporate the alcohol before incorporation into the ointment

Packaging of Ointments

- **Container/Closure**

  --Glass

  -Uncolored, colored, amber, blue, or opaque and porcelain-white

  -Light sensitive drugs?

  --Plastic

- **TUBES**

  --Tin or Plastic (can be laminated for stability)

  --Special Tips when ointments are used: Rectal, Ophthalmic, Vaginal, Aural

  --Ophthalmic Ointment Tubes: 1/8 oz. (3.5 g)

  --Topical Ointment Tubes: 5 g to 60 g

  --Tubes: -More convenient for patient

  -Ointment is less exposed to the environment

  -Store below 30°C to prevent softening

Packaging of Ointments

Official Ointments

- **Coal Tar Ointment, USP**
  --1% Coal Tar in Zinc Oxide Paste
  --Tween 80—aids incorporation Coal Tar into Base & enhances removal from skin when washed
  --Anit-eczematic
- **Hydrocortisone Ointment, USP (Cortril Oint., Pfizer)**
  --Contains 1% Hydrocortisone (Rx) and 0.5% (OTC)
  --Used as an Anti-inflammatory agent—short term use
- **Compound Undecylenic Acid Ointment, USP (Desinex, Pharmacraft)**
  --Contains 5% Undecylenic Acid and 20% Zinc Undecylenate in PEG Ointment Base
  --Topical Anti-fungal
- **Zinc Oxide Ointment, USP**
  --Used as Astringent (Zinc Oxide, Mineral Oil, White Ointment)

Ointments/Creams

- NOTE:
- An Ointment is a mixture of lipophilic materials (No water)
- Creams and Semi-Solid Emulsions contain water
- Some Creams are called Ointments because of the addition of an active ingredient to the cream base
- NO Ointments can be called creams

Creams

- **Definition: Semi-Solid Emulsion of O/W or W/O type used as bases or vehicles for drugs intended for topical use**
- **Requires heat because of high m.p. waxes present which add viscosity**
- **O/W Cream + > Water = Lotion**

General Method for Preparation of Creams

- 1. Heat oil soluble materials over steam bath until melted in evaporating dish or beaker
- 2. Heat water soluble materials to approximately same temperature (or a few degrees higher – why?) as in Step 1
- 3. Add water (2) to oil (1) with constant stirring
- 4. Remove container from heat, continue stirring until room temperature
- NOTE: Always add water phase to oil phase-Why?

Creams

- **<u>Cold Cream</u> (An Emulsion-like ointment):**

Rx: Spermaceti (Cetyl Esters Wax) 12.5 g
White Wax (Bleached Beeswax) 12.0 g
Mineral Oil 56.0 g
Sodium Borate 0.5 g
Purified Water 19.0 g

--Note: Emulsifying Agent results when sodium borate combines with free fatty acids present in the waxes (i.e. White wax contains Cerotic Acid and Spermaceti contains Cetyl Palmitate) – sodium soaps are the emulsifiers

--Phase-Volume Ratio determines the type of emulsion formed

--<45% water = W/O >45% Water = O/W

--Oils act as emollients (i.e. agents which soften the skin)

Steps:

1. **Mix & heat first three ingredients until melted (break wax into small pieces)**
2. **Dissolve Sodium Borate in Water—Heat**
3. **Add Water Phase to Oil Phase with stirring until cool. (Note: Continuous stirring yields soft prep, while if allowed to sit without stirring, hard prep results)**

Creams

- **Hydrophilic Ointment (Actually an O/W Emulsion):**

Rx:	MP	0.25 g
	PP	0.15 g
	SLS	10.0 g
	PG	120 g
	Stearyl Alcohol	250 g
	White Pet	250 g
	Purified water	370 g

--Emulsifying Agent is SLS (O/W)

--An emulsion type ointment easily washed from skin

--PG is humectant and hygroscopic, thus, retards water loss by evaporation (is less hygroscopic than glycerin)

Steps:

1. **Melt Oil Phase together (White Pet, Stearyl Alcohol)**
2. **Heat Water Phase (SLS, Water, Parabens, PG)**
3. **Add water phase to oil phase, Stir until cool, spatulate**

Creams

- **Vanishing Cream:**

Rx:	Stearic Acid		18 g
	Potassium Hydroxide		0.8 g
	Glycerin		5.0 g
	MP		0.1 g
	PP	0.01 g	
	Purified water	76.2 g	

Note: Emulsifying Agent is Potassium Stearate—O/W emulsion

--High water content

--By adding Silicone Oils to Creams—Causes the creams to disappear quicker into the skin by defoaming (decreasing the foam in the soap

--Could add perfume to cooled product

Pastes

- Definition: Ointment-like, intended for external use
- Contains large quantities of solids, thicker, stiffer than ointments
- Pastes are free of gritty particulates, and less greasy
- Generally more absorptive than ointments
- Levigating agent is always a portion of the base (i.e. rather than mineral oil)
- Remains in place on skin and absorbs moisture, thus preferred for oozing or weeping skin conditions
- Not suitable for application to hairy parts of the body

Official Pastes

- **Zinc Oxide Paste, USP**

  --Syn = Lassar's Plain Zinc Paste

  --Rx: **Zinc Oxide 25%**
  Starch 25%
  White Pet 50%

  --Levigate each powder with White Petrolatum, then mix

- **Zinc Oxide and Salicylic Acid Paste, USP**

  Rx: Salicylic Acid 2%
  Lassar's Paste 98%

- **Triamcinolone Acetonide Dental Paste, USP**
  - **Contains Triamcinolone Acetonide in suitable emollient paste.**

Gels

- **Definition: A semi-solid colloidal system in which the movement of the dispersion medium is restricted by an interlacing network of solvated particles**
- **For practical purposes, a gel can be considered to be a mixture of materials containing a significant amount of at least one liquid and a thickening agent which forms a non-pourable semi-solid**
- **There is a high degree of attraction—Gels like themselves**

Gels

- **Single Phase Gel**

  --Macromolecules distributed in such a manner that no boundaries exist between them and the liquid—Homogenously dispersed

- **Magmas or Milks**

  --Where the gel mass consists of floccules or small distinct particles of colloidal dimensions—"Polyphase"

Descriptive Terms Appropriate for Gels

- **Syneresis:**

  --When dispersion medium is squeezed out in the form of droplets because of the strong attraction between particles of the dispersed phase (glycerin, PG, sorbitol)

  --Thus: "Shake Well"

- **Thixotropy:**

  --A "gel to sol to gel" reversible phenomenon

  --Common with Veegum

  --semisolid—(shake)--liquid sol—(stand)--semisolid

Advantages of Gels

- Increasing number of cosmetic and pharmaceutical products in the form of transparent gels—"Elegant"
- Easy to remove from a container without waste
- Easily applied without dripping
- An attractive transparent appearance —"Esthetic"

Types of Gel Preparations

- **I. Organic Gels:**
  - **A. Anhydrous Systems**
    - **--Liquid paraffin or mineral oil + Gelling Agent**
    - **--Examples of gelling agents:**
      - **-Aluminum stearate**
      - **-Soaps**
      - **-Fumed Silica**
      - **-Polyamide resins**
      - **-Polyethylene**
    - **--Very difficult to prepare**
    - **--To prepare, heat oil and cool—very controlled**
    - **--Fumed Silica is a silica formed by vaporizing and then precipitating the gaseous silica on a cooled surface—Get a powder with a very small particle size and thus a very large surface area per unit volume**

Types of Gel Preparations

- **B. Aqueous or Hydro-alcoholic Systems**

  1. Prepared using surfactant blends

  (little or no use in Pharmacy)

  2. Using an Acrylic Polymer

  --Acrylic polymers used are a series of carboxyvinyl polymers—Carbopols

Types of Gel Preparations

- **Carbopols:**

  --Produce gels with few stability problems

  --Are organic acid polymers which form a low viscosity dispersion with an acid pH in water

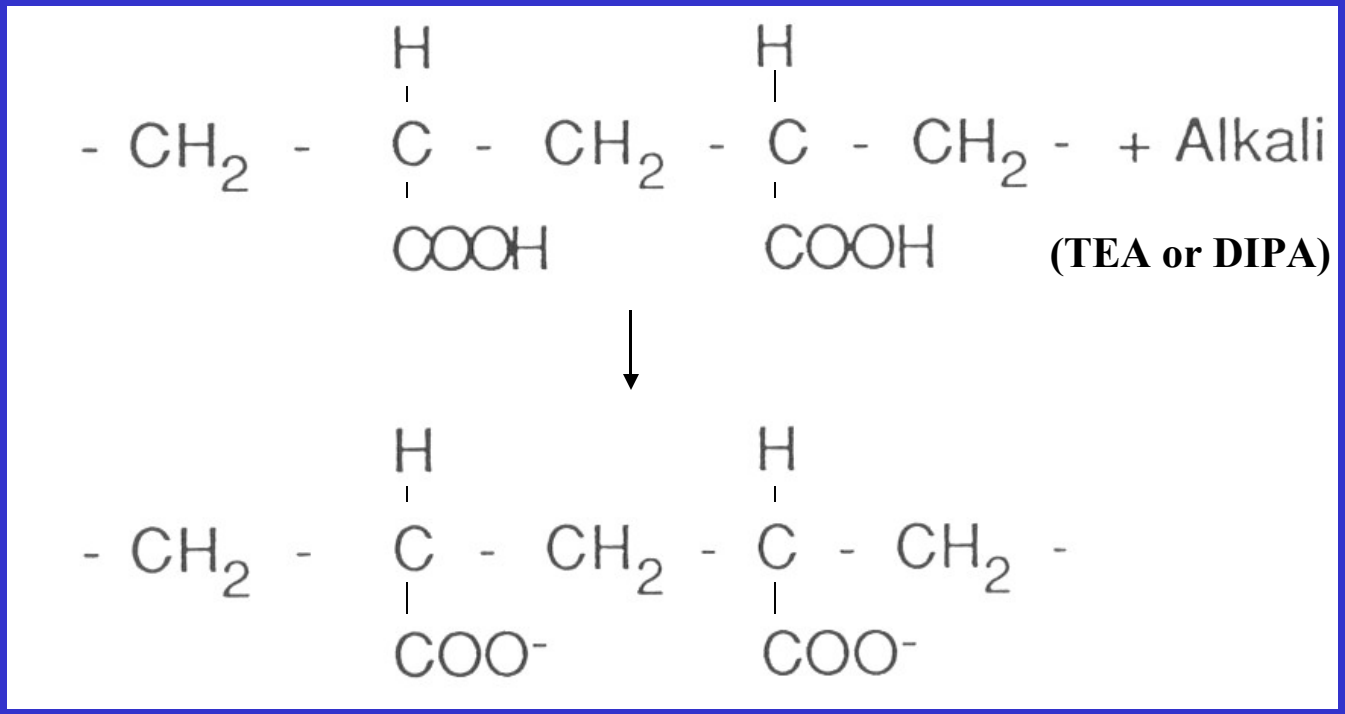
  --When the dispersion is neutralized by the addition of alkali, a gel is formed

  --Choice of neutralizing agent depends on whether the dispersion medium is aqueous or alcoholic

  -Water soluble alkali—Triethanolamine

  -Alcohol soluble amine--Diisopropranolamine

Carbopol Gel Reaction



(GEL)

Carbopol Dispersion Preparations

- Difficult to prepare
- Avoid Clumping

  --Add to water slowly in M&P with vigorous mixing
- Avoid Excess Alkali

  --Relationship between pH and viscosity

  --Excess alkali reduces viscosity

Types of Gel Preparations, cont.

- **II. Inorganic Gels:**
  - **--A number of 2-phase systems in which the gel is formed from inorganic materials**
  - **A. Bentonite Magma, USP**
    - **--Magma—Gel mass consisting of flocculates**
    - **--5% bentonite (colloidal hydrated aluminum silicate) in purified water**
    - **--Thixotropic Gel**
    - **--Use: Suspending Agent for I and E preps**
    - **--Bentonite swells to approximately 12 times its original volume in the presence of water**

Types of Gel Preparations, cont.

- **B. Veegum (magma), USP**
  - **--Colloidal hydrated magnesium aluminum silicate**
  - **--For comparison: 2% Veegum = 4% Bentonite**
  - **--Used for I and E preps**
  - **--Use: with high conc. of electrolytes or acidic preps - NO**

Jellies

- **Definition: Structurally similar to gels but they contain a higher content of liquid (i.e. water), and are usually less viscous**

  --Formed by adding a thickening agent to an aqueous solution of a drug

  --Subject to bacterial contamination

  --Warn patient to tightly close tube when not in use

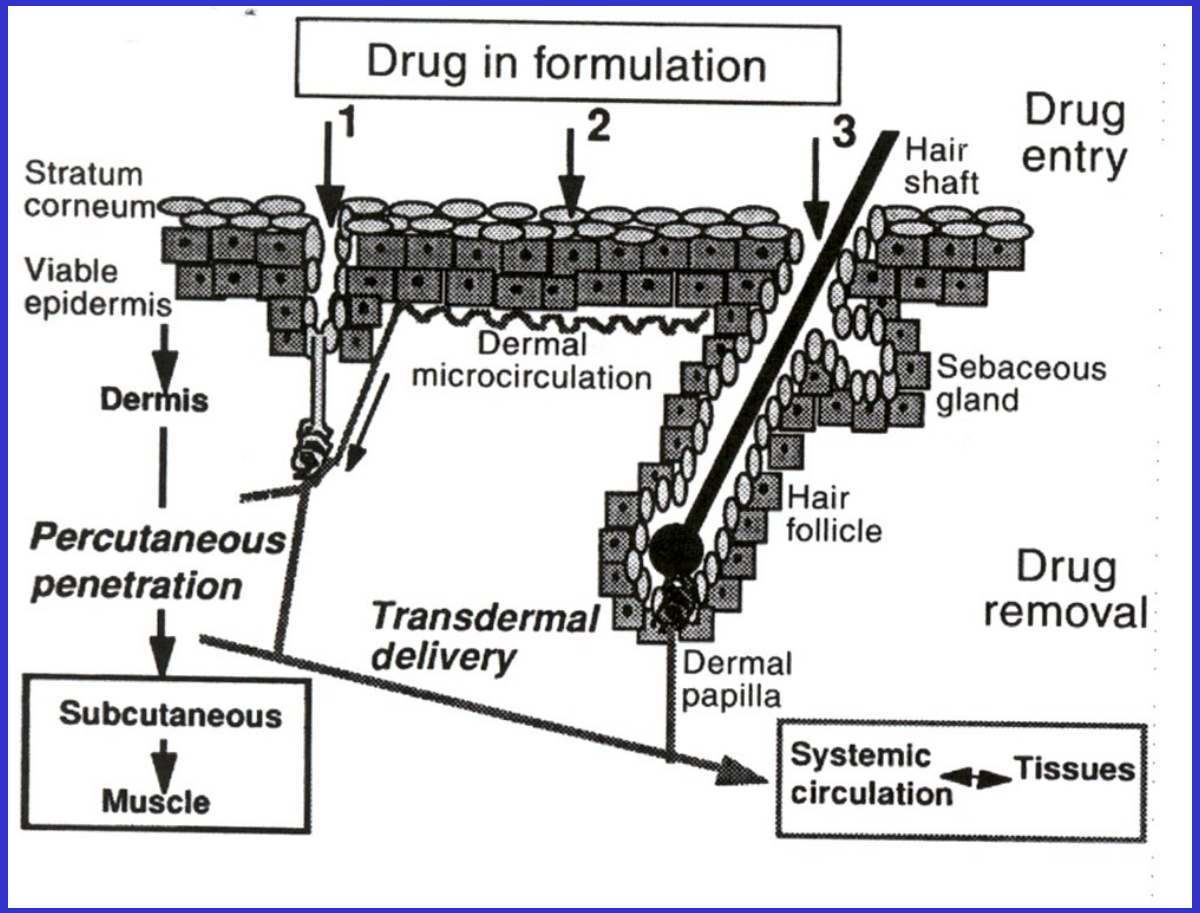
  --Official Preps:

  1. **Lidocaine HCl Jelly, USP—Topical Anesthetic (Urethritis)**
  2. **Phenylephrine HCl, nasal, USP**
  3. **Pramoxine HCl Jelly, USP—Topical Anesthetic (Rectal)**

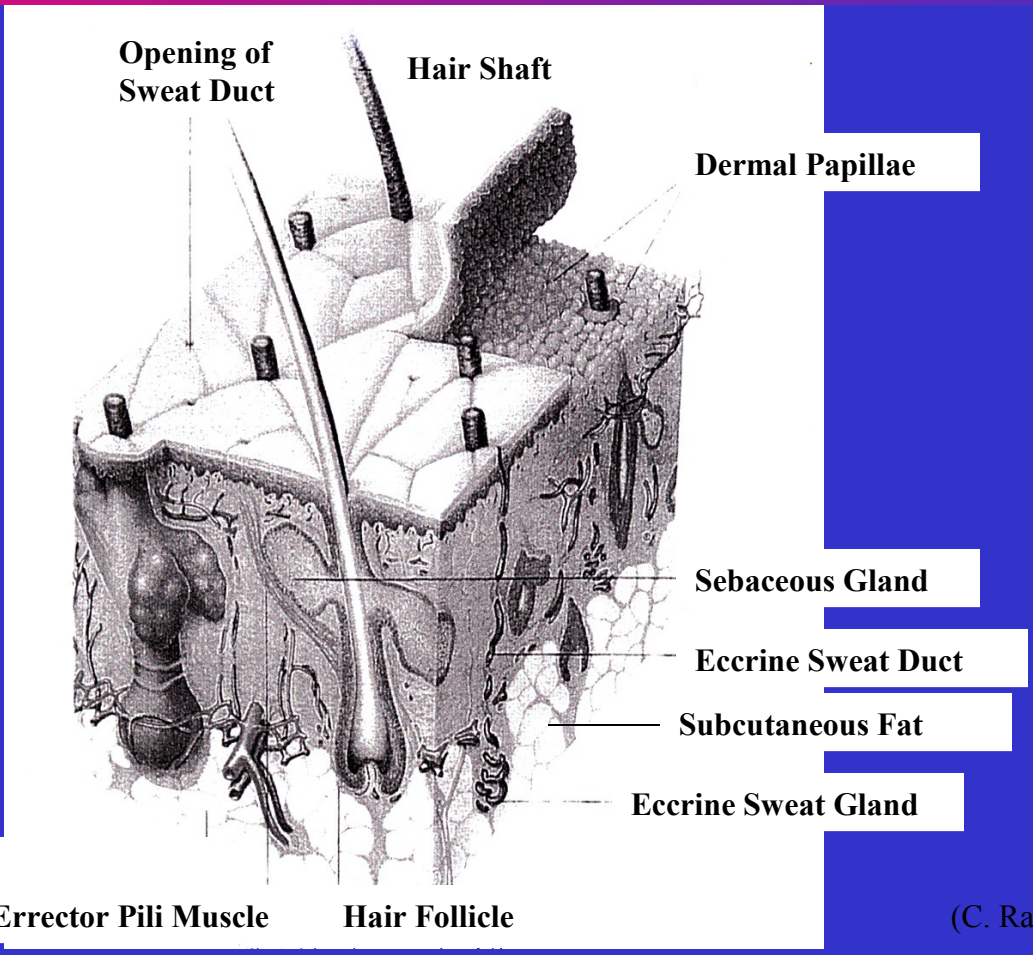
Supplemental Material

Absorption of Substances through the Skin

1. Sweat Ducts
2. Stratum corneum
3. Hair Follicles



Schematic Representation of the Human Skin



(C. Ramachandran, 2000)